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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/581,534

06/01/2006

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EXAMINER

WILLIS, DOUGLAS M

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

05/25/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/581,534 | Applicant(s) BURNS ET AL. | |
| | Examiner DOUGLAS M. WILLIS | Art Unit 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-12 and 14-28 is/are pending in the application.
- 4a) Of the above claim(s) 15-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-12, 14 and 21-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims / Priority

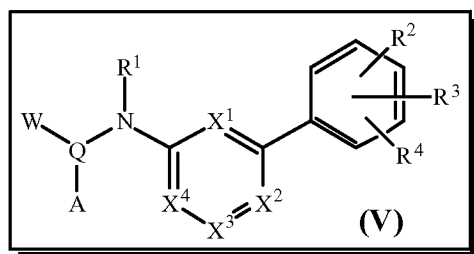
Claims 10-12 and 14-28 are pending in the current application. According to the *Claim Amendments*, filed April 15, 2010, claims 10-12 and 23-25 were amended and claims 1-9 and 13 were cancelled. This application is a 35 U.S.C. § 371 National Stage Filing of International Application No. PCT/AU2004/001689, filed December 3, 2004, which claims priority under 35 U.S.C. § 119(a-d) to AU 2003906680, filed December 3, 2003.

Status of Priority Objection - Priority Date

Applicant's arguments, on page 9 of the *Remarks*, filed April 15, 2010, with respect to AU 2003906680, filed December 3, 2003, have been fully considered, and are persuasive. Consequently, the objection to the priority date accorded AU 2003906680, made in the *Non-Final Rejection*, mailed on February 2, 2010, is hereby withdrawn.

Status of Restrictions / Election of Species

Applicant's affirmation of the following election, without traverse, in the reply filed on



April 15, 2010, is acknowledged: a) Group II - claims 10-12, 14 and 21-28, where X₁ = -N-; X₂ = -N-; X₃ = -C-; and X₄ = -C-; and b) substituted pyrimidine of formula (V) - p. 48, example 18.

The requirement was made FINAL in the *Non-Final Rejection*, mailed on February 2, 2010.

This application contains claims 15-20, drawn to nonelected inventions, without traverse,

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in the reply filed on April 15, 2010. A complete reply to the final rejection may include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.02.

The sections of U.S.C. Title 35 that formed the basis of prior rejections formulated, as well as any references supporting said rejections, that are not included with this Office action, may be found in the *Non-Final Rejection*, mailed on February 2, 2010. Furthermore, any rejections and/or objections of record not explicitly addressed herein below, are hereby withdrawn, in light of applicant's arguments and/or the *Claim Amendments*, filed April 15, 2010.

Thus, a second Office action and prosecution on the merits of claims 10-12, 14 and 21-28 is contained within.

Status of Claim Rejections - 35 U.S.C. § 112, First Paragraph

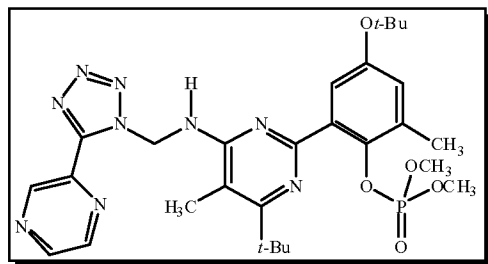
Applicant's arguments, on page 10 of the *Remarks*, filed April 15, 2010, with respect to claims 10-12, 14 and 21-28, have been fully considered, but are not persuasive. Consequently, the rejection of claims 10-12, 14 and 21-28, made in the *Non-Final Rejection*, mailed on February 2, 2010, is hereby maintained for the reasons of record.

Applicant primarily argues that since the nature of the *prodrug* has been specifically defined and is inherently reasonable, it is believed this basis for rejection has been overcome.

In response to applicant's argument that since the nature of the *prodrug* has been specifically defined and is inherently reasonable, it is believed this basis for rejection has been overcome, the examiner respectfully disagrees, since, the specification must teach how to make and use the invention, not teach how to figure out for oneself how to make and use the invention. {See *In re Gardner*, 166 USPQ 138 (CCPA 1970)}.

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Similarly, applicant's elected invention is directed to Group II, drawn to substituted pyrimidines and pharmaceutical compositions of the formula (V), where $X_1 = -N-$; $X_2 = -N-$; $X_3 = -C-$; and $X_4 = -C-$. Based on the guidance provided by the specification and, absent any evidence to the contrary, it is presently unclear whether a *prodrug* of a substituted pyrimidine of



the formula (V), such as 4-(*tert*-butoxy)-2-(4-(*tert*-butyl)-5-methyl-6-(((5-(pyrazin-2-yl)-1*H*-tetrazol-1-yl)-methyl)amino)pyrimidin-2-yl)-6-methylphenyl dimethyl phosphate, shown to the left, is either synthetically

feasible or possesses utility in the human body as a tubulin inhibitor.

The examiner requires that applicant: a) discretely indicate where the specification enables one of ordinary skill in the art to make the *prodrug* of the substituted pyrimidine of the formula (V), shown above, or a pharmaceutically acceptable composition thereof; and b) discretely identify enabling disclosure that will allow one of ordinary skill in the art to use the *prodrug* of the substituted pyrimidine of the formula (V), shown above, or a pharmaceutically acceptable composition thereof, as a tubulin inhibitor, to overcome this rejection.

Applicant should note that (a) it is not the function of claims to specify impossible or inoperative species {See *In re Anderson*, 176 USPQ 331 (CCPA 1973); and *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976)}, and that (b) a rejection under the first paragraph of 35 U.S.C. § 112 is proper if the claims contain a significant number of seemingly inoperative embodiments. {See *In re Corkill*, 771 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985); *In re Langer*, 503 F. 2d 1380, 183 USPQ 288 (CCPA 1974); and *Schering Corp. v. Gilbert*, 153 F.2d 428, 68 USPQ 84 (2d Cir. 1946), mod'g, *Schering Corp. v. Gilbert*, 67 USPQ 42 (SDNY 1945)}.

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Moreover, applicant should further note that the enablement requirement refers to the requirement of 35 U.S.C. § 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is that defined by the claims of the particular application or patent.

The purpose of the requirement that the specification describe the invention in such terms that one skilled in the art can make and use the claimed invention is to ensure that the invention is communicated to the interested public in a meaningful way. The information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention. A patent claim is invalid if it is not supported by an enabling disclosure.

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. {See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)}. Accordingly, even though the statute does not use the term *undue experimentation*, it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. {See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988); and *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d

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1217, 1223 (Fed. Cir. 1988)}.

Status of Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Applicant's arguments, on page 11 of the *Remarks*, filed April 15, 2010, with respect to claims 10, 14, 23, 24, 26 and 27, have been fully considered, but are not persuasive. Consequently, the rejection of claims 10, 14, 23, 24, 26 and 27, made in the *Non-Final Rejection*, mailed on February 2, 2010, is hereby maintained for the reasons of record.

Applicant primarily argues that the phrase *optionally substituted*, in connection with a 3-8 membered ring, has been deleted from the claims, thus obviating the rejection.

In response to applicant's argument that the phrase *optionally substituted*, in connection with a 3-8 membered ring, has been deleted from the claims, thus obviating the rejection, the examiner respectfully disagrees, since, according to the *Claim Amendments*, filed April 15, 2010, the phrase *optionally substituted 3-8 membered ring* is still present throughout claims 10 and 24.

The examiner suggests removal of the phrase *optionally substituted*, with respect to 3-8 membered ring and providing discrete substituents for each occurrence of *optionally substituted 3-8 membered ring*, to overcome this rejection.

New Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

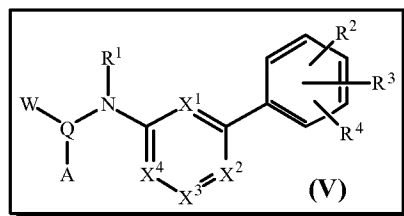
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cai, et al.

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in WO 02/047690.

The instant application recites substituted pyrimidines and compositions of the formula

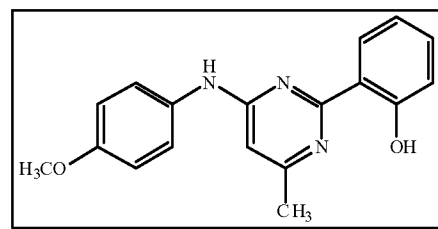


(V), shown to the left, where $X^1 = -N-$; $X^2 = -N-$; $X^3 = -CY-$, wherein $Y = -C_{1-4}alkyl$; $X^4 = -CY-$, wherein $Y = -H$; $Q = -a$ bond-; W is absent; $A = -aryl$, substituted with $p-OC_{1-4}alkyl$;

$R^1 = -H$; $R^2 = -OH$; $R^3 = -H$; and $R^4 = -H$, as tubulin inhibitors.

Cai, et al. (WO 02/047690) teaches substituted pyrimidines and compositions of the

formula (V), shown to the right, where $X^1 = -N-$; $X^2 = -N-$; $X^3 = -CY-$, wherein $Y = -CH_3$; $X^4 = -CY-$, wherein $Y = -H$; $Q = -a$ bond-; W is absent; $A = -phenyl$, substituted with $p-OCH_3$;



$R^1 = -H$; $R^2 = -OH$; $R^3 = -H$; and $R^4 = -H$, as activators of caspases and inducers of apoptosis {p. 13, ¶[0027], line 10; and pharmaceutical compositions - p. 9, ¶[0016]}.

Allowable Subject Matter

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DOUGLAS M. WILLIS, whose telephone number is 571-270-5757. The examiner can normally be reached on Monday thru Thursday from 8:00-6:00 EST. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DOUGLAS M WILLIS/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, AU 1624**